Applicants respectfully submit that none of the cited prior art references, neither in combination nor singly, teach or suggest the claimed invention as amended. Specifically, Claim 1 as amended sets forth that the diagnostic nucleotide is located <u>two</u> to four nucleotides from the 3' end of the reporter probe. Support for the amendment to Claim 1 can be found on Page 3, Line 30 to Page 4, Line 20 and Page 5, Line 22 to Page 6, Line 24 of the present application.

The diagnostic primer of amended Claim 1 is not taught or suggested by Krausa et al., since Krausa et al. do not teach a primer with diagnostic nucleotides located two to four nucleotides from the 3' end of the primer for purposes of detecting single nucleotide polymorphisms. Krausa et al. do not disclose a detector primer with the diagnostic nucleotide located two to four nucleotides from the 3' end of the diagnostic primer. Krausa et al. disclose detection of multi-nucleotide sequence differences between allelic variants, whereas the subject matter of Claim 1 is specific to the detection of single nucleotide polymorphisms.

Therefore, Applicants respectfully submit that one of ordinary skill would not have been motivated by the teaching of Krausa et al. to modify the primers of Newton et al. as allegedly suggested by Reynolds et al. to derive diagnostic primers having a diagnostic nucleotide <u>two</u> to four nucleotides 5' of the 3' end.

B. Claim 6 has been rejected under 35 U.S.C §103(a) as allegedly rendered unpatentable by Newton et al. in view of Reynolds et al and Krausa et al, and further in view of Mullis et al. (U.S. Patent No. 4,683,195).

The combination of Newton et al., Reynolds et al, and Krausa et al. do not teach or suggest the claimed invention as discussed above, and the secondary reference Mullis et al adds no further teachings which would enable one of ordinary skill in the art to achieve the claimed invention.

C. Claim 13 has been rejected under 35 U.S.C §103(a) as allegedly rendered unpatentable by Newton et al. in view of Reynolds et al and Krausa et al, and further in view of Guatelli et al (<u>Proc. Natl. Acad. Sci. USA</u>, <u>87</u>:1874-1878, 1990).

For the same reasons provided above, Applicants respectfully submit that none of the cited art teach or suggest the claimed invention and Guatelli et al. is a secondary reference that adds no further teachings which would enable one of ordinary skill to achieve the claimed invention.

D. Claims 19 and 20 were rejected under 35 U.S.C §103(a).as allegedly rendered unpatentable by Newton et al. in view of Reynolds et al. and Krausa et al. and further in view of Chen et al. (Nucleic Acids Research, 25(2): 347-353, 1997).

For the same reasons provided above, Applicants respectfully submit that none of the cited art teach or suggest the claimed invention, and Chen et al. is a secondary reference that adds no further teachings which would enable one of ordinary skill to achieve the claimed invention.

E. Claim 22 was rejected under 35 U.S.C §103(a) as allegedly rendered unpatentable by Newton et al. in view of Reynolds et al and Krausa et al, and further in view of Walker et al. (Nucleic Acids Research, 20(7): 1691-1696, 1992).

For the same reasons provided above, Applicants respectfully submit that none of the cited art teach or suggest the claimed invention, and Walker et al. is a secondary reference that adds no further teachings which would enable one of ordinary skill in the art to achieve the claimed invention.

Accordingly, in view of the above amendment and remarks, Applicants respectfully request withdrawal of the present rejections under Section 103.

Conclusions

The claims of the present application are believed to be in condition for allowance, and early notice thereof is respectfully requested. Attached hereto is a marked-up version of the changes made to the claims on the attached page entitled "Version with Markings to Show Changes Made".

Respectfully submitted,

Allan M. Kiang

Attorney for the Applicant

Registration No. 42,275

Becton Dickinson and Company 1 Becton Drive Franklin Lakes, New Jersey 07416 (201) 847-7111

#61597

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 1 has been amended as follows.

- 1. (2x Amended) A method for identifying a single nucleotide polymorphism in an isothermal target amplification reaction, said method comprising:
 - a) hybridizing a detector primer to the target, wherein the detector primer comprises a diagnostic nucleotide for the single nucleotide polymorphism, said diagnostic nucleotide located about [one] two to four nucleotides 5' of the 3' nucleotide of the detector primer which is complementary to the target sequence;
 - b) amplifying the target by hybridization and extension of the detector primer;
 - c) determining an efficiency of detector primer extension is greater, lesser or equal to the efficiency of extension of a detector primer without said diagnostic nucleotide; and
 - d) detecting the presence or absence of the single nucleotide polymorphism based on the efficiency of detector primer extension.